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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,492	03/31/2004	Rebecca E. Cahoon	BB1149USDIV	8578

23906 7590 06/20/2006

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EXAMINER	
COLLINS, CYNTHIA E	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 06/20/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,492	CAHOON ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *March 31, 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0105*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-28 and 31-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to an isolated polynucleotide comprising: (a) a nucleotide sequence encoding a polypeptide having cyclin delta activity, wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity to SEQ ID NO:18, or (b) the complement of the nucleotide sequence of (a). The claims are also drawn to a vector comprising said polynucleotide and a recombinant DNA construct comprising said polynucleotide operably linked to at least one regulatory sequence. The claims are additionally drawn to a method for transforming a cell with said polynucleotide, and a cell, plant and seed comprising said recombinant DNA construct.

The specification describes SEQ ID NO:17 as the nucleotide sequence comprising a portion of the cDNA insert in clone ceb.pk0049.h5 encoding a portion of a corn cyclin delta-2 protein, and SEQ ID NO:18 as the deduced amino acid sequence of a portion of a corn cyclin delta-2 protein derived from the nucleotide sequence of SEQ ID NO:17 (page 4). The

specification also describes the amino acid sequence set forth in SEQ ID NO:18 as having a BLAST pLog score of 65.22 as compared to, and 37% amino acid sequence similarity to, a cyclin delta-2 from *Nicotiana tabacum* (NCBI Identifier No. gi 4160298) (pages 22-23). The specification does not describe nucleotide sequences encoding a polypeptide having cyclin delta activity, wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity to SEQ ID NO:18.

The Federal Circuit has recently clarified the application of the written description requirement to nucleotide sequences. The court stated that "A description of a genus of cDNAs may be achieved by means of recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 1569; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

In the instant case Applicant has not described a representative number of species falling within the scope of the claimed genus, which encompasses numerous undisclosed and uncharacterized nucleotide sequences that encode polypeptides having cyclin delta activity and an amino acid sequence of at least 90% or 95% sequence identity to SEQ ID NO:18, nor the structural features unique to the genus.

Claims 27-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in

the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to an isolated polynucleotide comprising: (a) a nucleotide sequence encoding a polypeptide having cyclin delta activity, wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity to or comprising SEQ ID NO:18, or (b) the complement of the nucleotide sequence of (a), including an isolated polynucleotide comprising SEQ ID NO:17. The claims are also drawn to a vector comprising said polynucleotide and a recombinant DNA construct comprising said polynucleotide operably linked to at least one regulatory sequence. The claims are additionally drawn to a method for transforming a cell with said polynucleotide, and a cell, plant and seed comprising said recombinant DNA construct.

The specification discloses the isolation and sequencing of cDNA clones from cDNA libraries, including a library designated ceb5 comprising cDNA obtained from mRNA expressed in corn embryo 30 days after pollination (Example 1 pages 16-18). The specification also discloses the identification of ESTs encoding amino acid sequences having homology to cyclin proteins using BLAST searches (Example 2 page 18). The specification additionally discloses the structural characterization of ESTs encoding amino acid sequences having homology to cyclin delta-2 proteins, including SEQ ID NO:17, a nucleotide sequence comprising a portion of the cDNA insert in clone ceb.pk0049.h5 encoding a portion of a corn cyclin delta-2 protein (SEQ ID NO:18) (Example 5 pages 22-23). The specification does not disclose a specific use or function for SEQ ID NO:17, or for its encoded polypeptide, SEQ ID NO:18.

The claimed invention is not enabled because the function of a coding sequence cannot reliably be predicted on the basis of its structure or on the basis of the homology of its encoded amino acid sequence to other known sequences, as structural homology is not always indicative of functional homology.

See, for example, Whisstock J.C. et al. (Prediction of protein function from protein sequence and structure. Q Rev Biophys. 2003 Aug;36(3):307-40. Review), who teach

> "... prediction of protein function from sequence and structure is a difficult problem, because homologous proteins often have different functions. Many methods of function prediction rely on identifying similarity in sequence and/or structure between a protein of unknown function and one or more well-understood proteins. Alternative methods include inferring conservation patterns in members of a functionally uncharacterized family for which many sequences and structures are known. However, these inferences are tenuous. Such methods provide reasonable guesses at function, but are far from foolproof." (Abstract)

Whisstock J.C. et al. also teach at page 309 that while the observation that similar sequences determine similar structures gives us general confidence in homology modeling, much less reliable is the widely held assumption that proteins with very similar sequences should by virtue of their very similar structures have similar functions. Whisstock J.C. et al. further teach at page 309 that to reason from sequence and structure to function is to step on much shakier ground, that while many families of proteins contain homologues with the same function, the assumption that homologues share function is less and less safe as the sequences progressively diverge, and that even closely related proteins can change function through divergence to a related function or by recruitment for as very different function in such cases the assignment of function on the basis of homology in the absence of direct experimental evidence will give the wrong answer.

Whisstock J.C. et al. additionally teach at page 310 that a protein need not even change sequence to change function, as numerous proteins exhibit multiple functions in different cellular environments such that even if detailed in vitro studies on isolated proteins do identity a function we cannot be sure we know the molecules full repertoire of biological activities, and that nonhomologous proteins may conversely have similar functions.

Whisstock J.C. et al. further teach that while general hints based on protein sequence, structure, genomics and interaction patterns may be useful in guiding experimental investigations of protein function,

> "inferring protein function from knowledge of the function of a close homologue is like solving the clue of an American crossword puzzle. Finding the word that satisfies the definition may be difficult but the task in principle is straightforward. Working out the function of a protein from its sequence and structure is like solving the clue of a British crossword puzzle. It is by no means obvious which features of the definition are providing the real clues, as opposed to misleading ones. Also, for both types of puzzle and for the suggestion of a protein function, even if your answer appears to fit it may be wrong." (pages 311-312).

The claimed invention is also not enabled because the function of a polynucleotide cannot be reliably predicted on the basis of a partial encoded amino acid sequence, since a polypeptide expressed from such a polynucleotide may require the presence of specific amino acids or amino acid domains in order to function, which amino acids or domains may not be present in a partial amino acid sequence.

See also, for example, Renaudin J.P. et al. (Plant cyclins: a unified nomenclature for plant A-, B- and D-type cyclins based on sequence organization. Plant Mol Biol. 1996 Dec;32(6):1003-18. Review), who teach that CycD cyclin polypeptides have specific structural features that may have functional significance. Renaudin J.P. et al. teach that in the CycD1 class of plant cyclins, the leucine in the LxCxE motif essential for cyclin D-associated kinases to bind

to and phosphorylate Rb is directly preceded by an acidic amino acid, whereas there is an intervening residue in CycD2 and CycD3, and that the consensus sequence of this whole region is different in CycD1 and CycD3, differences that they suggest could be indicative of the existence of multiple Rb-like proteins having different affinities for CycD groups in plants. Renaudin J. et al. also teach that a region of variable length and low homology is located carboxy terminal to the Rb-binding region of plant D-type cyclins, and that all CycD3 sequences have a valine in place of the tyrosine that is present in the highly conserved KYEE motif in helix H3 in mitotic cyclins, whereas CycD1 and CycD2 plant D-type cyclins have a methionine at this position. Renaudin J. et al. additionally teach that plant CycD cyclin polypeptides have at least one potential PEST sequence believed to be responsible for rapid proteolysis in the N-terminal and/or C-terminal part of the polypeptide. (page 1010 column 1 last paragraph to page 1011 second column first paragraph)

In the instant case the specification does not provide guidance with respect to which polynucleotides comprising a nucleotide sequence encoding a polypeptide having an amino acid sequence of at least 90% or 95% sequence identity to or comprising SEQ ID NO:18 encode a polypeptide having cyclin delta activity and which do not. Absent such guidance one skilled in the art would have to clone from corn and/or isolate from undisclosed sources and/or synthesize the claimed polynucleotides, and then test each one for cyclin delta activity, in order to determine which polynucleotide sequences, if any, exhibit cyclin delta activity and which do not. Such a trial and error approach to practicing the claimed invention would constitute undue experimentation.

Claim Rejections - 35 USC § 101 and 112

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-36 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The claims are drawn to an isolated polynucleotide comprising: (a) a nucleotide sequence encoding a polypeptide having cyclin delta activity, wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity to or comprising SEQ ID NO:18, or (b) the complement of the nucleotide sequence of (a), including an isolated polynucleotide comprising SEQ ID NO:17. The claims are also drawn to a vector comprising said polynucleotide and a recombinant DNA construct comprising said polynucleotide operably linked to at least one regulatory sequence. The claims are additionally drawn to a method for transforming a cell with said polynucleotide, and a cell, plant and seed comprising said recombinant DNA construct.

The specification discloses the isolation and sequencing of cDNA clones from cDNA libraries, including a library designated ceb5 comprising cDNA obtained from mRNA expressed in corn embryo 30 days after pollination (Example 1 pages 16-18). The specification also discloses the identification of ESTs encoding amino acid sequences having homology to cyclin proteins using BLAST searches (Example 2 page 18). The specification additionally discloses

the structural characterization of ESTs encoding amino acid sequences having homology to cyclin delta-2 proteins, including SEQ ID NO:17, a nucleotide sequence comprising a portion of the cDNA insert in clone ceb.pk0049.h5 encoding a portion of a corn cyclin delta-2 protein (SEQ ID NO:18) (Example 5 pages 22-23). The specification does not disclose a specific use or function for SEQ ID NO:17, or for its encoded polypeptide, SEQ ID NO:18.

The claimed invention is not supported by a well established utility because the claimed subject matter is not known in the prior art.

The claimed invention is not supported by a specific and substantial asserted utility because no specific and substantial utility is asserted or established for the claimed subject matter.

While the specification at pages 11-15 suggests that the disclosed polynucleotides and their encoded polypeptides would find a number of uses, such as to isolate CDNAS and genes encoding homologous proteins, in polymerase chain reaction protocols to amplify longer nucleic acid fragments, in the design of synthetic peptides to facilitate immunological screening of CDNA expression libraries, to create transgenic plants, as a targets to facilitate design and/or identification of inhibitors of their encoded enzymes that may be useful as herbicides, and as probes for genetically and physically mapping genes and as markers for traits linked to those genes, the specification does not disclose any specific use of SEQ ID NO:17 or its encoded polypeptide (SEQ ID NO:18), for example to isolate a particular CDNA or gene, to amplify a particular nucleic acid fragment, in the design of particular synthetic peptides and immunological screening of a particular CDNA expression library, to create transgenic plants having particular properties, as a target to facilitate design and/or identification of a specific inhibitor of SEQ ID

NO:18, or as probe to genetically and physically map a particular gene or as a marker for a particular trait linked to a particular gene.

Also, while the specification classifies the polypeptide encoded by SEQ ID NO:17 as a cyclin delta-2 protein, such a classification based on amino acid sequence homology does not establish a specific use or function for the claimed sequence of SEQ ID NO:17 or SEQ ID NO:18, because the structural classification of an encoded polypeptide as a member of a particular class of proteins, such as a cyclin delta-2 protein, does not establish a specific and substantial utility for the polynucleotide or for its encoded polypeptide, since sequence and structural homology between different amino acid sequences is not necessarily correlated with functional homology. See, for example, Whisstock J.C. et al., set forth above.

Additionally, the prior art discloses no specific and substantial use for the amino acid sequence that SEQ ID NO: 18 is disclosed as being homologous to (Sorrell, D.A. et al. GenBank Accession No. CAA09852, cyclin D2.1 protein [*Nicotiana tabacum*], GI:4160298, January 15, 1999).

The disclosed uses are not specific to the subject matter claimed (SEQ ID NO:17 or SEQ ID NO:18), but are generally applicable to the broad class of invention claimed (nucleic acids encoding polypeptides). The disclosed uses are also not substantial, as further characterization of the claimed subject matter would be required to identify or reasonably conform a real world use for SEQ ID NO:17 or SEQ ID NO:18.

Claims 27-36 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a

well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Remarks

No claim is allowed.

Claims 27-36 are deemed free of the prior art of record, due to the failure of the prior art to teach or suggest an isolated polynucleotide comprising: (a) a nucleotide sequence encoding a polypeptide having cyclin delta activity, wherein the polypeptide has an amino acid sequence of at least 90% or 95% sequence identity to or comprising SEQ ID NO:18, or (b) the complement of the nucleotide sequence of (a), including an isolated polynucleotide comprising SEQ ID NO:17.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR

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Cynthia Collins
Primary Examiner
Art Unit 1638

CC

Cynthia Collins
6/12/06